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PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC/4-33529A	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/EP2004/013589	International filing date *(day/month/year)* 30.11.2004	Priority date *(day/month/year)* 01.12.2003
International Patent Classification (IPC) or national classification and IPC C07C237/22, A61K31/165		
Applicant NOVARTIS AG et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05.09.2005	09.01.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Rufet, J Telephone No. +49 30 25901-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/013589

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-31 as originally filed

   Claims, Numbers

   1-10 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4-6,10
	No:	Claims	1-3,7-9
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V.

1. Reference is made to the following documents:

D1: TETRAHEDRON LETTERS, vol. 42, 2001, p. 4819-4823, XP004247360
D2: EP-A-0 678 503 (CIBA-GEIGY AG)
D3: EP-A-1 215 201 (SPEEDEL PHARMA AG)
D4: WO 02/40007 A (NOVARTIS AG)

2. Novelty

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-3, 7-9 is not new in the sense of Article 33(2) PCT in view of the teaching of D1.
Document D1 discloses compounds falling under the scope of present claim 1 (see especially compounds 1a and 9a on p. 4821 and p. 4822, column 1, paragraph 1) which are potent human renin inhibitors (see p. 4819, column 1, first paragraph).

2.2 Documents D2-D4 refer to structurally very close renin inhibitors which differ from the compounds of present claim 1 by the nature of the substituent R^9, which is different than hydrogen. It is also stressed that in D2, see formula (II), R^9 could be a hydroxy group having a protecting group, whereby in this case the moiety -NH-R^8 as claimed in the current application is not given in formula (II).

3. Inventive step

3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 4-10 does not involve an inventive step in the sense of Article 33(3) PCT.

Starting from the closest prior art D1, the problem underlying the present application should be seen in the provision of **further** delta-amino-gamma-hydroxy-omega-aryl-alkanoic acid amides which are potent human renin inhibitors, since there is no biological information in the present application showing that the compounds of claims 4-6 have improved properties if compared to the closest compounds of D1.

In view of the technical information given in D1 the proposed solution to the abovementioned problem according to claim 4-6 is considered to be obvious, since the derivatisations made on the compounds of claims 4-6 belong to the common practice within the field of chemistry.
The skilled person would have, with expectation of success, applied such derivatisations known from D1 on the compounds of D2-D4 as an alternative, if he wanted to provide further delta-amino-gamma-hydroxy-omega-aryl-alkanoic acid amides having enzyme renin inhibiting properties.

3.2 However, the breadth of the claims should be such that it could be expected that all the compounds comprised by the subject-matter of these claims would actually solve the problem underlying the invention.
According to that, it is noted that expressions like "esterified or amidated carboxy", "heteroaryl" or "aryl" on claim 1 are speculative in the sense of Article 33(3) PCT, embracing a great variety of structural possibilities not yet explored by the Applicant, the effect of which cannot be foreseen having regard to the problem to be solved.
The breadth of the claims should be such that it could be expected that all the compounds comprised by the subject-matter of these claims would actually solve the problem underlying the invention.
Moreover the proposed definitions for the substituent X being O, NH, S, SO or SO_2 appear not to represent a reasonable generalisation over the results put forward; since only derivatives with X being $-CH_2-$ having been made and tested (see p. 8, l. 3-5) and from D2 only -CH2- and -CH(OH)- appears to be known equivalent groups.